EFFICACY REVIEW
BY KEVIN J. SWEENEY, ENTOMOLOGIST

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Team Reviewer: Bonaventure Akinlosutu

EPA Reg. No. 2724-LNU

Registrant: Wellmark International

Product Manager: George LaRocca, PM13

Dec # 355865

DP#: 316838

Product Name: RF2004 (CCSO)

Active ingredient: 40% etofenprox and 3.6% s-methoprene

Formulation: RTU cat spot-on

Sites: cats

Pests: fleas, ticks and mosquitoes

OPPTS Guideline: 810.3300
GLP? Yes as indicated below.

Request: Evaluate efficacy data submitted in support of cat spot-on product performance claims. Efficacy data were not cited.

Study Submitted:
MRID 46513410 Summary Report on RF2004 (CCSO) Development (non-GLP)
MRID 46513411 GLP Efficacy Against Adult Cat Fleas of Formulation RF2004 (CCSO) (GLP)
MRID 46513412 Efficacy Against cat Fleas of a RF2004(CCSO) Formulation.(non-GLP)
MRID 46513413 Efficacy Comparison Against Adult Cat Fleas of Sergeant's Gold Squeeze-On and a Variation of RF2004 (CCSO). (Non-GLP)
MRID 46513414 Efficacy Comparison Against Adult Cat Fleas of a Variation of RF2004 (CCSO) when Cats are Kept in Larger Enclosures. (non-GLP)
MRID 46513415 GLP Repellency and Efficacy Against Adult Mosquitoes and Ticks on cats of Formulation RF2-004 (CCSO) (GLP).

Summary of the Results from the Submitted Studies

The submitted data included non-GLP and GLP efficacy studies where in-vivo and in-vitro data were collected. The target dose of etofenprox was 231.1 mg/kg of cat. The effective product application rates were 1.0 to 3.0 ml per animal depending on the weight of the cat.

Pest	Method	Days of 90% or greater control	Etofenprox dose delivered in product formulation unless otherwise noted expressed in mg/kg	Application Volume per cat
Mosquitoes [1] (Aedes and Culex spp.)	Caged in-vivo	18	400 mg of etofenprox per cat weighing under 9 lbs. 600 mg of etofenprox applied to a cat weighing 9 lbs or more.	1.0 – 1.5 ml (0.9941 g and 1.49115 g)
Black-legged [1] tick	in-vitro with treated hair	100% at day 7 89% at day 32	Same as for mosquitoes	Same as for mosquitoes
American dog [1] tick	Caged in-vivo	11 days	Same as for mosquitoes	Same as for mosquitoes
Adult Flea [2&3]	in-vivo	28 days --caged-- 21 days --caged-- 16 days --caged-- 16 days --caged-- 23 days penned -	205 mg/kg 108 - 129 mg/kg 110 mg/kg 266 mg/kg of etofenprox without product carrier 266 mg/kg of etofenprox without product carrier	1.5 – 3.0 ml 1.0 – 2.0 ml 1.0 – 1.5 ml

Footnotes:

1. Dose for this study was expressed in volume and total number of grams applied per cat. A rate stated as mg of ethofeprox per kg of cat was not calculated and stated. The value stated here is calculated by EPA from the study methods. Half of the cats weighted 5-9 lbs (2.27 kg – 4.09 kg) and the other half weighed 9 to 17 lbs (4.09 kg – 7.73 kg). This should have resulted is an etofenprox dose range in the lower weight group of 176.6 mg/kg – 97.7 mg/kg and in the higher weight group 146.6 mg/kg – 77.61 mg/kg.

The average dose rate was not stated and the groups were mixed when the results were reported. In fact the 17 lbs cat was not listed in the results. However, in the study tables summarizing the data for mosquito and tick testing there were 5 cats in each group. In the lower weight group the average weight was 7.8 lbs. or 3.54 kg yielding an average dose of etofenprox of 400mg/3.54 kg = 112.99 mg/kg of cat. In the higher weight group the average weight was 9.98 lbs. or 4.53 kg yielding an average dose of 600mg/4.53kg = 132.54 mg/kg of cat. Note that both these values are well below the target dose of 231 mg etofenprox /kg of cat.

These data show that when cats are dosed at up to 132.54 mg of etofenprox/kg of cat the product provides: 1) only 18 days of repellency protection against mosquitoes based on blood-feeding success of questing female mosquitoes exposed to cats; 2) 11 days of control against the American dog tick exposed to cats; and 3) in the in-vitro testing with Ixodes sp. (black-legged ticks) exposed to treated cat hair (fur) 100% control at 24 hours post-exposure on day 7, 50% control at 24 hours post-exposure day 32 and 89% at 48 hours post–exposure on day 32. To achieve a higher degree of efficacy more product is required per animal.

2. The registrant argues that the carrier in the formulation is tied to the residual efficacy of the product. Tests were conducted with and without the carrier. Comparative testing was also done with the Sergeant's registered product formulation containing 55% etofenprox. The subject product performed better than the registered product in these studies.

3. For control of flea larva and eggs, at least 1.0 ml of product is required per animal as this is the lowest dose rate stated on 2724-488, a product with the same % of pyriproxifen.

Entomologist's Recommendations

1. The submitted efficacy testing for the subject product when applied according to draft label directions supports the following claims for mosquitoes: Repels mosquitoes for up to 18 days. From the draft label the following mosquito claims are acceptable: "Direct on-animal protection for mosquitoes." The rest of the claims should be modified or deleted in accordance with the data.

2. The submitted efficacy testing for the subject product when applied according to draft label directions supports label claims for black-legged ticks only of up to one-month.

3. The submitted efficacy testing for the subject product when applied according to draft label directions supports the label claims for fleas with control of one-month.

4. The reapplication interval of once per month supports the flea and black-legged tick claims only.

5. The acceptance of the above claims is based on the dose rates used in these studies. If the product animal safety data results require a lower product application rate for safety reasons, then the labeled directions for use of this product should be revisited based on the doses discussed in the efficacy table and footnotes above.